Journal of Surgical Oncology 1998;68:199–203

Acquired Hypertrichosis Lanuginosa: Case Report and Review of the Literature

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Acquired hypertrichosis lanuginosa is a rare cutaneous disorder usually associated with internal malignancy that consists of the development of abnormal hair growth of the lanugo type, often confined to the skin of the face and neck, although other areas also may be involved. We report on a 66-year-old woman with a metastatic ductal infitrating carcinoma of the breast who developed growth of fine lanugo type hair on her face and progressive growth of the hair of eyebrows and eyelashes. We review the literature on this uncommon paraneoplastic cutaneous disorder emphasizing the pathogenic mechanisms that have been proposed to explain the striking overgrowth of lanugo type hair.

J. Surg. Oncol. 1998;68:199–203.

KEY WORDS: **paraneoplastic syndromes; lanugo type hair overgrowth; trichomegaly of eyelashes**

INTRODUCTION

Acquired hypertrichosis lanuginosa (AHL) is a rare condition first reported by Turner [1] in 1865 in a patient with breast cancer. Since 1865, approximately 50 cases have been described in the literature, usually associated with malignant diseases [2,3]. Malignant neoplasms more frequently associated with AHL include lung cancer [4–17] and colorectal carcinomas [18–28], but it has also been described in association with lymphomas [29,30] as well as carcinomas of the kidney [31], pancreas [32], breast [1,33–35], uterus [29,36,37], ovary [38], bladder [39], gallbladder [40], leukemia [41], and liver metastatic adenocarcinoma [42]. In women with AHL, the more frequent malignancy is colorectal cancer, followed in order of frequency by lung cancer and breast cancer; in men, lung cancer is the malignancy most frequently associated with AHL, followed by colorectal cancer.

We report a new case of AHL associated with carcinoma of the breast. The patient also had trichomegaly of the eyelashes and eyebrows. We review the literature on AHL (Table I).

CASE REPORT

A 66-year-old woman had a history of breast carcinoma in the left breast, which was excised 35 years before; the patient received postsurgery radiotherapy. An endometrial carcinoma was surgically excised 6 years before. She was admitted in our hospital because of chest pain and electrocardiographic anomalies that were considered secondary to heart compression by a mediastinic mass. An erythematous plaque on the right breast areola was histopathologically examined and a diagnosis of mammary Paget's disease was established. Subsequently, an infiltrating ductal carcinoma of the right breast was discovered. The neoplasm extended to the anterior mediastinum. Six months later, the patient had severe pleural effusion. She received treatment with torsemide, amiodarone, omeprazole, ticlopidine, and lorazepam. Dermatologic consultation was obtained be-

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Accepted 16 April 1998

TABLE I. Review of the Literature on AHL and Associated Malignacy*

Author, year [ref.]	Age (years)/sex	Associated malignancy	Associated manifestations
Turner, 1865 [1]	42/F	Breast	—
Lyell and Whittle, 1951 [39]	35/F	Bladder carcinoma	—
Dingley and Marten, 1957 [38]	56/F	Ovary adenocarcinoma	Glossitis, skin change, weight loss
Fretzin, 1967 [4]	69/M	Lung anaplastic carcinoma	Glossitis, skin change, weight loss
Herzberg et al., 1969 [40]	65/M	Gallbladder carcinoma	—
Hensley and Glynn, 1969 [5]	41/M	Lung undifferentiated adenocarcinoma	Skin change, weight loss, taste/smell change
Chadfield and Khan, 1970 [18]	78/F	Rectum adenocarcinoma	Diarrhea
Djajadiningrat et al., 1970 [19]	43/F	Rectum adenocarcinoma	—
Hegedus and Schorr, 1972 [20]	45/F	Colon poorly differentiated carcinoma	Diarrhea, glossitis, weight loss
	56/F	Colon mucinous adenocarcinoma	—
Van Der Lugt and Dudok De Wit, 1973 [21]	73/F	Colon adenocarcinoma	Diarrhea, glossitis, taste/smell change
Anderson, 1973 [6]	63/M	Lung squamous carcinoma	Glossitis, taste/smell change
Samson et al., 1975 [29]	66/F	Uterus	—
	35/F	Lymphoma	—
Rzempoluch et al., 1976 [7]	44/F	Lung anaplastic carcinoma	Glossitis, skin change, weight loss
Kaiser et al., 1976 [36]	46/F	Uterus adenocarcinoma	Weight loss
Wadskov et al., 1976 [33]	54/F	Breast solid carcinoma	Diarrhea, glossitis, skin change
Reinhold et al., 1974 [22]	60/F	Cecum adenocarcinoma	Weight loss
McLean and Macaulay, 1977 [32]	19/F	Pancreas islet cell carcinoma	Diarrhea, weight loss
Ikeya et al., 1978 [8]	69/M	Bronchus undifferentiated large cell carcinoma	Diarrhea, glossitis, skin change, weight loss
Davies et al., 1978 [23]	59/F	Sigmoid colon carcinoid	Weight loss
Ricken, 1979 [41]	24/F	Chronic lymphocytic leukemia	Skin change
Goodfellow et al., 1980 [10]	61/M	Lung polygonal cell carcinoma	Glossitis, skin change, weight loss, taste/smell change
González et al., 1980 [9]	71/M	Lung, bladder transitional cell carcinoma	Glossitis, weight loss
Shee and Graham, 1981 [11]	57/M	Lung adenocarcinoma	Diarrhea, glossitis, weight loss
Knowling et al., 1982 [12]	62/M	Lung adenocarcinoma	Glossitis, weight loss
	57/F	Lung adenocarcinoma	Weight loss
Sindhuphak and Vibhagool, 1982 [42]	32/F	Liver, metastatic adenocarcinoma	Glossitis, skin change, weight loss
Ulrich and Munk-Jensen, 1983 [13]	34/F	Lung solid carcinoma	Glossitis, taste/smell change
George et al., 1983 [34]	46/F	Breast infiltrating duct carcinoma	—
Price and Hall-Smith, 1985 [24]	63/F	Sigmoid colon	Glossitis
Kassis et al., 1985 [37]	54/F	Endometrium, lung anaplastic adenocarcinoma	—
Jemec, 1986 [30]	48/F	Small cell follicular lymphoma	Glossitis, weight loss
Skaf and Anthony, 1986 [25]	62/F	Ascending colon adenocarcinoma	Glossitis, weight loss
Hoveden, 1987 [14]	76/F	Lung clear cell carcinoma	Diarrhea, glossitis, weight loss
Dyall-Smith et al., 1987 [26]	48/M	Colon adenocarcinoma	Diarrhea, glossitis, skin change, weight loss, taste/smell change
Carratalá et al., 1987 [15]	69/F	Lung adenocarcinoma	—
Mengori and Rosales, 1989 [27]	69/M	Colon adenocarcinoma	Diarrhea, weight loss
Rodríguez et al., 1990 [16]	30/F	Lung transitional cell carcinoma	Glossitis, skin change, weight loss
Salazar et al., 1990 [17]	50/M	Lung undifferentiated carcinoma	Glossitis, skin change, weight loss, taste/smell change
De Clercq et al., 1990 [35]	58/F	Breast ductal carcinoma	Glossitis, taste/smell change
Duncan and Hemming, 1994 [31]	69/M	Renal cell carcinoma	—
Brinkmann et al., 1992 [28]	30/M	Colon carcinoma	—
Present case	66/F	Breast	—

*Modified from Hoveden [2].

cause of the progressive overgrowth of eyebrows and eyelashes, which showed longer and profuser hair shafts (Fig. 1), as well as fine and whitish lanugo hair on the cheeks, chin, nose, and ears (Fig. 2). Hair shafts of similar characteristics were also present on the thighs and arms. No signs of virilization or hirsutism were seen and axillary and pubic hair were normal. Laboratory investigations, including full blood count, disclosed the follow-

Fig. 1. Trichomegaly of eyelashes and increased growth of eyebrows.

ing anomalies: leukocytosis of 16.000 leukocytes/mm^3, hemoglobin 10.8 g/dl, platelets 374.000/mm^3, total proteins 5.7 g/dl, albumin 2.8 g/dl, and γ-glutamyltransferase 78 U/l. Hormonal determinations showed the following results: dehydroepiandrosterone 300 ng/ml (N: 80–1.000 ng/ml), basal 17OH-progesterone 1.7 ng/ml (N < 1 ng/ml), follicle stimulating hormone 24.8 mU/ml (N: 25–145 mU/ml), luteinizing hormone 12.1 mU/ml (N: 17–71 mU/ml), prolactin 42.3 ng/ml (N: 4–20 ng/ml), estradiol 39 pg/ml (N < 25 pg/ml), free testosterone 1 pg/ml (N: 2–5 pg/ml), and androstenedione 1.8 ng/ml (N: 1–4 ng/ml); thyroid stimulating hormone, free T4, and T3 were normal. In addition, we determined tumor markers with the following results: carcinoembryonic 4.5 ng/ml (N: 0–4 ng/ml), antigens CA 15.3 15 U/ml (N: 0–30 U/ml), CA 19.9 5 U/ml (N: 0–35 U/ml), and CA 125 64 U/ml (N: 0–35 U/ml).

The patient developed widespread metastatic disease and died 2 months later.

DISCUSSION

AHL is a rare paraneoplastic condition characterized by the development of lanugo type hair, with thin, non-pigmented hair shafts that can reach unusual length. It is usually located on the face, within eyebrows and eyelashes, on the forehead, ears, and nose. It may also appear over the trunk, axillae, and limbs; it usually spares the palms, soles, suprapubic, and genital areas [3].

AHL may be associated with several manifestations, including burning glossitis [8,12,13,29,33], papillary hypertrophy of the tongue [20], disturbances of taste [40] and smell, diarrhea [18,31], adenopathy, and weight loss [2], and other skin anomalies such as scleroderma [17], acanthosis nigricans [10,38], and seborrheic keratoses [30].

Several laboratory abnormalities have been reported in association with AHL, although no consistent findings have yet been identified. In some patients, AHL has been associated with high levels of gonadotropin, CEA, serum calcium, serum gastrin, urinary cortisol, as well as low levels of testosterone [2].

Hegedus et al. [20] published a histopathologic study of AHL, describing lanugo hair follicles extending almost parallel to the epidermal surface, and many of these follicles were of the so-called mantle type, containing immature sebocytes within the mantle epithelium. Our patient showed similar histopathologic features, but the follicles were arranged perpendicularly to the epidermal surface.

Human hair differentiates into lanugo, vellous, and terminal hair types. Lanugo hair develops during the period from the end of the 3rd month of fetal life to the 7th month, and then it is shed before birth. Vellous hair is seen over the face and arms of children, and is shorter, softer, and usually non-pigmented. It appears in the 8th month of intrauterine life. Terminal hair is found on the scalp, eyebrows, and eyelashes from birth, and in the beard, axillae, pubis, and trunk of some adults. It changes from vellous hair follicles with age and under the influence of androgens. It is longer and coarser than vellous pigmented hair and, characteristically, terminal hair is medullated [14]. Several pathogenic mechanisms, such as secretion of humoral substances by the tumor which stimulate the development of lanugo hairs, have been proposed to explain AHL, but no consistent findings have been identified.

Differential diagnoses include hirsutism and hypertrichosis associated with drugs, such as cyclosporin, streptomycin, penicillin, phenytoin, spironolactone, diazoxide, minoxidil, interferon, and corticosteroids, and hypertrichosis associated with shock, thyrotoxicosis, porphyrias, Hurler syndrome, and Cornelia de Langes' syndrome. Our patient had no history of treatment with any drug related with hypertrichosis and the hormonal study, as well as the clinical picture, ruled out the diagnosis of hirsutism.

Trichomegaly of eyelashes was first reported by Casanova et al. [43] associated with acquired immunodeficiency syndrome (AIDS). Since then several cases have been described in the literature, both associated and not associated with AIDS. In this latter group, cases of trichomegaly have been recorded in a patient who received recombinant leukocyte A interferon for non-Hodgkin lymphoma [44] and in patients receiving cyclosporin A [45]. Some authors proposed an immunologic mechanism as the cause of trichomegaly of eyelashes. Other authors postulated severe malnutrition as the etiologic factor of trichomegaly. Vélez et al. [46] reported a patient

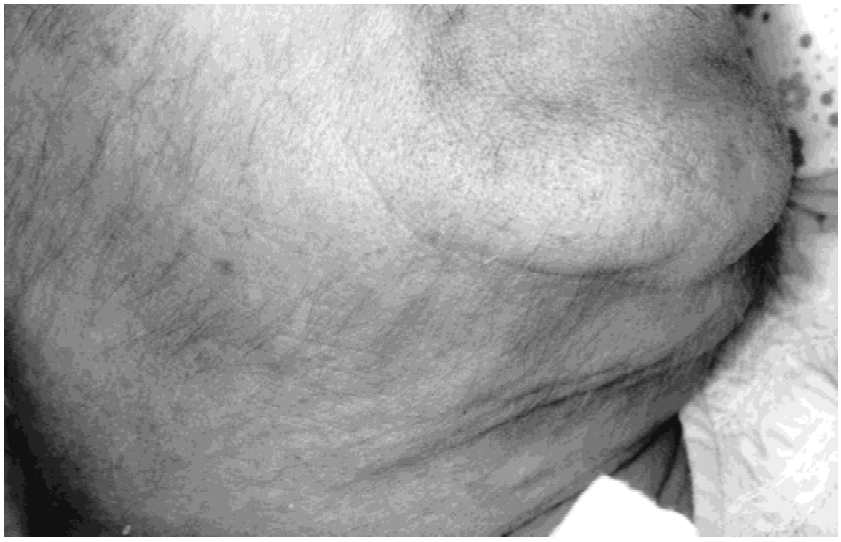

Fig. 2. Clinical picture showing fine and white lanugo hair on the cheeks and chin.

with metastatic renal adenocarcinoma who developed trichomegaly of eyelashes and hypertrichosis of terminal hair probably associated with malnutrition. In our patient, the overgrowth of lanugo type hair was not related to signs of virilization and therefore a diagnosis of AHL seems to be the most appropriate.

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